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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/650,474	08/28/2003	Chen Chen	690068.589C1	6139

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EXAMINER

COLEMAN, BRENDA LIBBY

ART UNIT PAPER NUMBER

1624

DATE MAILED: 11/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/650,474

Applicant(s)

CHEN ET AL.

Examiner

Brenda L. Coleman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-10 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-10 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 1/04.
- 4) ☐ Interview Summary (PTO-413),
Paper No(s)/Mail Date. ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: ____.

DETAILED ACTION

Claims 1-10 are pending in the application.

Claim Rejections - 35 USC § 112

1. Claims 1-7 and 9 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The scope of claim 1-7 and 9 are not adequately enabled solely based on inhibitory effect on corticotrophin releasing factor provided in the specification. Claims 1 and 2 are directed to the method of treating any and all diseases and/or disorders associated with hypersecretion of corticotrophin releasing factor, which is not remotely enabled. The scope of claims 1-7 and 9 includes diseases and/or disorders not even known at this time, which may be associated with inhibitory effect on corticotrophin releasing factor. While treatment of seizures, infantile spasms, etc. have been linked with inhibitory effect on corticotrophin releasing factor, the art does not recognize use of such inhibitors as broad based drugs for treating all disorders instantly embraced.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

2. Claims 1-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

- a) Claims 1 and 2 provides for the use of the compounds of formula I, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.
- b) Claims 1, 3 and 5-10 are vague and indefinite in that it is not known what is meant by a "thiomorpholinyl group" in the definition of R⁵ and R⁶ taken together with the nitrogen atom.
- c) Claims 1-10 are vague and indefinite in that it is not known what is meant by "naphtyl" in the definition of Ar¹.
- d) Claim 3 is vague and indefinite in that it is not known what is meant by formula (I-1) where no formula labeled formula (I-1) appears in the claim.
- e) Claim 9 is a substantial duplicate of claims 3-6, as the only difference is a statement of intended use, which is not given material weight. Note In re Tuominen 213 USPQ 89.
- f) Claims 1-7 and 9 are vague and indefinite in that the claim provides for the use of claimed compounds, but the claim does not set forth any steps involved in determining, which are the physiological disorder capable of being modulated by inhibiting an activity of corticotrophin releasing factor. It is unclear which diseases are mediated by corticotrophin releasing factor". Determining whether a given disease responds or does not respond to such an inhibitor will involve undue experimentation. Suppose that a given drug, which has inhibitor properties in vitro, when administered to a patient with a certain disease, does

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not produce a favorable response. One cannot conclude that specific disease does not fall within this claim. Keep in mind that:

A. It may be that the next patient will respond. No pharmaceutical has 100% efficacy. What success rate is required to conclude our drug is a treatment? Thus, how many patients need to be treated? If "successful treatment" is what is intended, what criterion is to be used? If one person in 10 responds to a given drug, does that mean that the disease is treatable? One in 100? 1,000? 10,000? Will the standard vary depending on the current therapy for the disease?

B. It may be that the wrong dosage or dosage regimen was employed. Drugs with similar chemical structures can have markedly different pharmacokinetics and metabolic fates. It is quite common for pharmaceuticals to work and or be safe at one dosage, but not at another that is significantly higher or lower. Furthermore, the dosage regimen may be vital --- should the drug be given e.g. once a day, or four times in divided dosages? The optimum route of administration cannot be predicted in advance. Should our drug be given as a bolus iv or in a time release po formulation. Thus, how many dosages and dosage regimens must be tried before one is certain that our drug is not a treatment for this specific disease?

C. It may be that our specific drug, while active in vitro, simply is not potent enough or produces such low concentrations in the blood that it is not an effective treatment of the specific disease. Perhaps a structurally related drug is potent enough or produces high enough blood concentrations to treat the

disease in question, so that the first drug really does fall within the claim. Thus, how many different structurally related inhibitors must be tried before one concludes that a specific compound does not fall within the claim?

D. Conversely, if the disease responds to our second drug but not to the first, both of which are inhibitors in vitro, can one really conclude that the disease falls within the claim? It may be that the first compound result is giving the accurate answer, and that the success of second compound arises from some other unknown property, which the second drug is capable. It is common for a drug, particularly in thrombosis, to work by many mechanisms. The history of psychopharmacology is filled with drugs, which were claimed to be a pure receptor XYX agonist or antagonist, but upon further experimentation shown to affect a variety of biological targets. In fact, the development of a drug for a specific disease and the determination of its biological site of action usually precede linking that site of action with the disease. Thus, when mixed results are obtained, how many more drugs need be tested?

E. Suppose that our drug is an effective treatment of the disease of interest, but only when combined with some totally different drug. There are for example, agents in antiviral and anticancer chemotherapy, which are not themselves effective, but are effective treatments when the agents are combined with something else.

Consequently, determining the true scope of the claim will involve extensive and potentially inconclusive research. Without it, one skilled in the art cannot determine the actual scope of the claim. Hence, the claim is indefinite.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3. Claims 1 and 2 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1, 3, 4 and 6-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Markwell et al., U.S. Patent No. 4,833,136. Markwell teaches the method of use of the compounds of formula (I) where R¹ is NR⁵R⁶, R² is methyl, R³ is phenyl, 4-chlorophenyl, 3-methoxyphenyl or 4-methoxyphenyl, R⁴ is hydrogen, R⁵ is hydrogen, and R⁶ is -CH₂-CH₂-OH, -CH₂-CH=CH₂ or isobutyl. See examples 3, 5, 6, 7 and 8.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Markwell et al., U.S. Patent No. 4,833,136. The generic structure of Markwell encompasses the instantly claimed compounds (see Formula I, column 1) and for the same use as claimed herein. Examples 3 and 5-8, etc., which anticipates the method of use of the instant invention differ only in the nature of the R₀, R₁, R₂, R₃, R₄ and R_x substituents. Column 1, line 52 through column 2, line 40 defines the R₀, R₁, R₂, R₃, R₄ and R_x substituents. Some of the preferred embodiments of Markwell include where R₀ is hydrogen, methyl, ethyl, n- and iso-propyl, preferably hydrogen (see lines 43-44, column 2), R₁ and R₂ include hydrogen and methyl (see line 45, column 2), R₃ is n-butyl, prop-2-enyl, 2-hydroxyethyl, 3-dimethylaminopropyl and 3-diethylaminopropyl (see lines 5-8, column 3), R₄ is hydrogen or C₁₋₄ alkyl (see line 29, column 2) and R_x is phenyl and phenyl substituted with chloro, hydroxy or methoxy (see lines 24-26, column 3). The compounds of the instant invention are generically embraced by Markwell in view of the interchange ability of R₀, R₁, R₂, R₃, R₄ and R_x substituents of the bicyclic ring system. Thus, one of ordinary skill in the art at the time the invention was made would have been motivated to select for example 2-hydroxyphenyl or 3-chlorophenyl as well as other possibilities from the generically disclosed alternatives of the reference

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and in so doing obtain the instant compounds in view of the equivalency teachings outlined above.

6. Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al., EP 0 773 023. The generic structure of Chen encompasses the instantly claimed compounds (see Formula II, page 2) and for the same use as claimed herein.

Examples on page 5, lines 35-42 differ only in the nature of the E and Y substituents.

Page 3, lines 4-8 defines the D, E and Y substituents where D is: (i) N or -CR₁₀ when a double bond connects E and D and E is -CR₄; (ii) -CR₁₀ when a double bond connects E and D and E is N; (iii) -CR₈R₉, -CHR₁₀, -C=O, -C=S, -C=NH, or -C=NCH₃ when a single bond connects E and D; E is -CR₄ or N when a double bond connects E and D, and E is -CR₄R₆ or -NR₆ when a single bond connects E and D; and Y is N or -CH. The compounds of the instant invention are generically embraced by Chen in view of the interchange ability of D, E and Y substituents of the bicyclic ring system. Thus, one of ordinary skill in the art at the time the invention was made would have been motivated to select pyrazolo[4,3-b]pyridine as well as the substituents of the bicyclic ring system from the generically disclosed alternatives of the reference and in so doing obtain the instant compounds in view of the equivalency teachings outlined above.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated

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by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 1-9 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-15 of U.S. Patent No. 6,613,777.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the compounds, compositions and method of use of the compounds of formula I are embraced by the compounds, compositions and method of use of the compounds of formula I of U.S. '777 where R³ is naphthyl or optionally substituted phenyl or pyridyl.

Claim Objections

8. Claims 8 and 10 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim must be in the alternative. See MPEP § 608.01(n).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda L. Coleman whose telephone number is 571-272-0665. The examiner can normally be reached on 9:30-6:00.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Brenda L. Coleman
Primary Examiner Art Unit 1624
November 23, 2005